REMARKS

Claims 1. 7 and 18 are herein amended, and claims 3-5, 8, and 9 are pending as filed. Support for these amendments can be found throughout the specification as filed, and specifically at page 14, lines 24-32, page 15, lines 1-32, page 16, lines 1-32, page 17, lines 1-5, page 20, lines 30-32, and page 21, lines 1-31; at page 10, lines 26-29, page 11, lines 19-23, page 19, lines 24-32, and page 20, lines 1-22; at page 10, lines 4-20, page 12, lines 13-15, page 19, lines 4-23, and page 20, lines 23-28; and at page 9, lines 11-23, page 12, lines 28-32, page 13, lines 1-8, and page 17, lines 6-16.

Rejections under 35 U.S.C. §112

Scope of Enablement

Pending claims 1, 3-5, 7-9 and 18 stand rejected under 35 U.S.C § 112, first paragraph for failure to provide a disclosure sufficient to enable the claims.

While not acceding to the grounds of the rejection asserted in the Office Action, Applicants have amended the claims in view of this ground of rejection. Specifically, Applicants have amended independent claims 1 and 7 to incorporate the psychotropic, neurotropic, neurological drugs, antibiotic, antibacterial, antimycotic, antiviral, antiproliferative and antineoplastic drugs set forth explicitly in claims 2 and 8 (respectively) that have been cancelled. Applicants have also amended claims 1 and 7 to recite the amino acids and amino acid derivatives previously recited in claims 6 and 10 (respectively) that have been cancelled. Applicants respectfully contend that these amendments overcome the asserted ground of rejection under 35 U.S.C. § 112, first paragraph. Applicants thus respectfully request that the Examiner withdraw this rejection.

In addition, the Action sets forth a rejection based on conjugates of combinations of different drugs with the amino acids or derivatives thereof that target the drugs to physiologically protected sites. Applicants respectfully contend that the claims recite conjugates of individual drugs with an amino acid or a derivative thereof that transport the drugs to a physiologically-protected site. Applicants respectfully contend that there is nothing in the language of the claims that would lead one of ordinary skill in the art to envision pharmaceutical compositions comprising *mixtures* of different drugs conjugated to said targeting amino acid or derivative thereof, nor does the specification disclose such

combinations. Applicants would appreciate any clarification the Office could provide in the basis for this rejection if it is not withdrawn as a consequence of the amendments submitted herein.

Indefiniteness

Claims 1, 3-5, 7-9 and 18 stand rejected under 35 U.S.C. §112, second paragraph as being indefinite. While not acceding to the grounds of the rejection asserted in the Office Action, Applicants have amended independent claims 1 and 7 to recite specific amino acids and derivatives comprising the pharmaceutical compositions encompassed by the claims. Applicants respectfully contend that the amendments overcome the asserted ground of rejection under 35 U.S.C. §112, second paragraph. Applicants thus respectfully request that the Examiner withdraw this rejection.

Improper Markush Group

Claims 1, 4-5, 7, and 18 stand rejected for employing an improper Markush group. While not acceding to the grounds of the rejection asserted in the Office Action, Applicants have amended the claims to avoid reciting Markush language, and Applicants respectfully contend that the amendments overcome the rejection. Applicants respectfully request that the rejection be withdrawn.

Claims 1 and 7 have been amended to more clearly delineate those components of the invention that should be grouped together. Applicants believe that the members belonging to the first named component of the composition (namely, "psychotropic, neurotropic or neurological drug, or an antibiotic, antibacterial, antimycotic, antiviral, antiproliferative or antineoplastic drug") are properly grouped under component "a". These members all are biologically-active drugs delivered according to the invention to physiologically protected areas in the body.

The second component is "an amino acid or amino acid derivative," which, in the current invention, is used to target the drug to the physiologically protected area in the body. There is no teaching that this amino acid or amino acid derivative itself plays any role other than delivering the drug recited in "a" to the physiologically protected site.

Applicants respectively contend that these amendments overcome rejection of claims 1 and 7 for reciting an improper Markush group, and that thus dependent claims 4, 5, and 18 are also free of this ground of rejection. Accordingly, Applicants thus respectfully ask the Examiner to withdraw this ground of rejection.

Rejections under 35 U.S.C. §102(b)

Anticipation

Claims 1, 3-5, 7-9, and 18 stand rejected under 35 U.S.C §102(b) as being anticipated by U.S. Patent No. 5,149,794 ("Yatvin I"), pending claims 1, 3-5, 7-9, and 18 stand rejected under §102(b) as being anticipated by U.S. Patent No. 5,543,389 ("Yatvin II"); and pending claims 1, 3-5, 7-9, and 18 stand rejected under §102(b) as being anticipated by U.S. Patent No. 5,827,819 ("Yatvin III"). Applicants respectfully traverse.

The basis for a rejection for anticipation is that each and every limitation in the claimed invention is taught in a single prior art reference. The prior art cited in the Office Action does not teach the invention as currently claimed. All of the Yatvin patents cited in the Office Action require that a polar lipid be *covalently* attached to a drug, either directly through linker functional groups or via a spacer, where the polar lipid facilitates the targeted delivery of the drug. For instance, Claim 1 of Yatvin I claims "A composition of matter comprising an antiviral or antineoplastic drug, **a polar lipid carrier**, two linker functional groups and a spacer, wherein the spacer has a first end and a second end and **wherein the polar lipid is attached to the first end of the spacer through a first linker functional group** and the antiviral or antineoplastic drug is attached to the second end of the spacer through a second linker functional group." As disclosed in the Yatvin I specification, the linkage is a covalent linkage.

In contrast, the instantly-claimed invention comprises a *specific* amino acid derivative covalently attached to a drug, wherein the amino acid derivative, *not a lipid,* targets the drug to a physiologically protected site, and a lipid is not recited as being a component of the invention at all.

Furthermore, in the Yatvin patents the spacer can be a peptide of formula $(\text{amino acid})_n$, wherein n is an integer between 2 and 25. The amino acid-containing structure disclosed in the Yatvin patents was provided as a spacer group, not as a targeting moiety.

Specifically, the amino acid or polymeric embodiments thereof taught in the Yatvin patents could be any amino acid, since the amino acid functioned solely as a spacer group, and was not an amino acid that was "specifically transported into a physiologically-protected site," as required in the pending claims. There is no teaching in the Yatvin patents to choose any particular amino acid other than in consideration of its properties as a spacer (for example, by embodying a cleavage site for release of the compound *in vivo*).

In the instantly-claimed invention, the amino acid derivative is covalently attached to the drug (directly or via a spacer) and is capable of targeting the attached drug to a physiologically protected site in the body. The amino acid or derivative thereof is explicitly recited in the amended claims as 5-hydroxytryptophan, serotonin, or melatonin. The formulae of the amino acids of the Yatvin patents do not anticipate the amino acid derivatives in the current invention, since one skilled in the art could not "at once envisage" the three named amino acid derivatives from the Yatvin patent teachings. Moreover, the recited amino acid derivatives do not fall within the scope of the Yatvin teachings of the spacer, having formula $(\text{amino acid})_n$ where the spacer is comprised of a polymer of a single amino acid. Thus, the current invention is structurally very different from the polar lipid conjugates disclosed in the earlier-filed Yatvin patents. Accordingly, none of the Yatvin patents anticipates the claims as currently pending. Applicants thus request that the Examiner withdraw this ground of rejection.

Obviousness-type double patenting rejection

Pending claims 1, 3-5, 7-9, and 18 stand rejected under the judicially created doctrine of obviousness-type double patenting over Yatvin I, Yatvin II, and Yatvin III.

The Office Action asserts that the instant claims would be obvious to one skilled in the art in light of the Yatvin patents. Applicants respectfully disagree. The Yatvin patents disclose the use of a polar lipid carrier to facilitate transport of a drug to a targeted site in the body. In contrast, the pending claims recite pharmaceutical compositions comprising a drug and particular amino acid derivatives that transport the drugs to physiologically protected sites. There is no teaching, suggestion or motivation in the cited art first, to provide compositions lacking a polar lipid carrier nor second to substitute amino acids or derivatives thereof for the polar lipids disclosed in the cited art

nor third to use the specific amino acid derivatives explicitly recited in the pending claims. There is no evidence of record that the skilled worker would expect that the polar lipid carriers taught by the Yatvin patents could be exchanged for the particular amino acid derivatives recited in the instant claims, particularly in view of the vast differences in structure, functions and chemical properties between polar lipids and these amino acid derivatives. Applicants thus respectfully contend that the cited art does not render the instantly-claimed invention obvious. Applicants respectfully request that the Office provide any evidence pursuant to 37 C.F.R. §1.104(d)(2) that polar lipids and amino acids would be considered interchangeable by one of ordinary skill in the art, so that Applicants can have the opportunity to address this evidence.

In the absence of any evidence of record that one or ordinary skill would be motivated to exchange the polar lipids taught in the prior art for the specific amino acid derivatives recited in the pending claims (since there is clearly no teaching nor suggestion to make such a substitution in the cited art), Applicants request that the Examiner withdraw this ground of rejection.

CONCLUSION

Applicants respectfully request the reconsideration of this application, and earnestly solicit a favorable determination of patentability of all pending claims.

If the Examiner in charge of this application believes it to be helpful, Applicants invite the Examiner to contact their undersigned representative by telephone at (312) 913-0001 in order to expedite the prosecution of this application.

Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff

Dated: October 27, 2004

By: _____
Kevin E. Noonan
Reg. No. 35,303